REMARKS

Accompanying the Amendment is a Petition for Revival of an Application for Patent Abandoned Unintentionally Under 37 C.F.R. 1.137(b). Applicants respectfully request entry of the Amendment and reconsideration of the outstanding rejections of the claims. Upon entry of the Amendment, claims 11, 31, 32, 34, 37, 38, 40-44, and 57-59 are pending in the present application.

Applicants have amended claims 11, 37, and 40. The amendments are supported throughout the specification including at page 10, lines 5-13, and at page 41, lines 32-33.

Claims 57-59 are newly presented. Applicants submit the new claims are supported throughout the specification, including at page 10, line 19, and at page 22, lines 16-25, and does not raise any issues of new matter.

Specification/Informalities

As suggested by the Examiner, the title of the application has been amended to "Antibody Against Human Sodium-Dependent Phosphate Cotransporter".

Claim Objections

The Examiner objected to claims 37, 38, 40, and 41 as being dependent upon a non-elected claim. As suggested by the Examiner, claims 37 and 40 have been amended to be independent claims and are no longer dependent on a non-elected claim. Applicants, therefore, respectfully request withdrawal of the objection.

Rejection of Claims Under 35 U.S.C. § 101

The Examiner rejected claims 11, 31, 32, 34, 37, 38, and 40-43 under 35 U.S.C. § 101 as not supported by either a specific and substantial asserted utility or a well established utility. Applicants respectfully traverse the rejection.

The Examiner maintains the asserted utility of the claimed antibodies is not substantial or specific because the instant specification does not disclose a substantial or specific utility for the

polypeptide of SEQ ID NO:1 or any information linking the polypeptide of SEQ ID NO:1 to a specific disease state that could be treated or diagnosed using the claimed antibody. Applicants respectfully traverse the rejection.

According to the USPTO Utility Guidelines, specific utility is that which is specific to the subject matter claimed. Thus, specific utility requires more than a statement of general utility for diagnosing an unspecified disease. A more specific statement of specific conditions that can be treated or diagnosed can satisfy this requirement. According to the USPTO Utility Guidelines, a substantial utility is that which defines a "real world" use. Courts have found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an "immediate benefit to the public" and satisfies the utility requirement. MPEP § 2107.01(III); *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995). Applicants submit that the claimed invention has a specific and substantial utility.

First, given the chemical and structural homology between a polypeptide having an amino acid sequence of SEQ ID NO: 1 and human renal sodium phosphate transport protein (NPT1; GI 450532), Applicants assert specific utility is based on the known function of NPT1, namely transport of phosphate molecules across cellular membranes. Homology to sequences of known function is a commonly used and reliable technique in the art for elucidating function. See Brenner et al., 1998, *Proc. Natl. Acad. Sci.*, 95:6073-6078. Forty percent sequence identity has been found to be a reliable threshold for determining homology for sequence alignments of at least 70 residues. Thirty percent sequence identity has been found to be a reliable threshold for determining homology for sequence alignments of at least 150 residues. See Brenner et al., supra, at 6076. In view of this, Applicants submit that determining sequence identity to a known structure, such as NPT1, is a well-established technique for determining homology between the polypeptides.

The polynucleotide encoding the polypeptide of SEQ ID NO: 1 was isolated from a renal cell carcinoma that had metastasized to the brain. The polypeptide of SEQ ID NO: 1 shares 48% sequence identity over 402 amino acids with NPT1. See specification, page 10 at lines 28-33. Forty-eight percent homology over 402 amino acids exceeds Brenner et al.'s reliability threshold for determining homology. Additionally, the polypeptide of SEQ ID NO: 1 has a similar

hydrophobicity plot to NPT1 and shares potential N-glycosylation sites with NPT1 at N_{49} and N_{92}. See specification, page 10 at lines 28-39 and Figures 3A and 3C. Therefore, Applicants submit that a polypeptide comprising the amino acid sequence of SEQ ID NO: 1 has specific utility as a transporter of phosphate molecules.

Secondly, the invention as claimed has many specific utilities disclosed in the specification. The specification discloses that antibodies that specifically bind to a polypeptide comprising SEQ ID NO: 1 are useful in diagnostic assays, and as antagonists or inhibitors. For example, at page 30, line 11, the specification describes the use of antibodies to NAPTR to diagnose conditions or diseases characterized by expression of NAPTR or to monitor patents being treated with NAPTR, agonists, antagonists or inhibitors. Examples of disorders associated with decreased expression of NAPTR include cancer of the kidney, tumoral calcinosis, osteomalacia, osteoporosis and others as described at page 31, lines 27-33. Examples of conditions associated with increased expression of NAPTR include abnormal phosphate regulation in neurons and gastrointestinal tract and liver, hypocalciuria, and hypocalcemia. ELISA assays are taught for detection of altered NAPTR expression in fluids or tissues from patient biopsies. See page 32, lines 1-6. In addition, the specification discloses that antibodies, which are specific for NAPTR, may be used directly as an antagonist or indirectly as a targeting or delivery mechanism for bringing a pharmaceutical agent to cells or tissues, which express NAPTR. See the specification at page 22, lines 20-25.

Based on the forgoing, Applicants have demonstrated that the specification provides specific and substantial utility for a polypeptide comprising the amino acid sequence of SEQ ID NO: 1. Applicants submit that a polypeptide comprising the amino acid sequence of SEQ ID NO: 1 has specific utility as a transport molecule for phosphate molecules. In addition to being useful in the purification of a polypeptide of SEQ ID NO: 1, Applicants have established that antibodies specific for a polypeptide comprising the amino acid sequence of SEQ ID NO: 1 may be used for the diagnosis of conditions or disease associated with expression of a polypeptide comprising SEQ ID NO: 1 and administered to treat or prevent disorders associated with increased phosphate levels, including hypocalciura and hypocalcemia. These utilities are specific to the subject matter claimed and define a "real world" use.

For at least these reasons, Applicants respectfully request withdrawal of the 35 U.S.C. § 101 rejection.

Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 11, 31, 32, 34, 42, and 43 under 35 U.S.C. § 112, second paragraph, as indefinite. The Examiner maintains the scope of the term "biologically active" as used in claim 11 is vague. Claims 31, 32, 34, 42, and 43 depend from claim 11. The term "biologically active" has been deleted from claim 11. Therefore, withdrawal of the rejection is respectfully requested.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

1. Enablement

The Examiner rejected claims 11, 31, 32, 34, 37, 38, and 40-43 under 35 U.S.C. § 112, first paragraph, as not enabled by the specification. The Examiner contends that one skilled in the art would not know how to use the claimed invention because the claimed invention is not supported by a specific and substantial asserted utility or a well established utility. In addition, the Examiner asserts that even if utility is established for antibodies specific for SEQ ID NO: 1, the specification does not reasonably provide for antibodies to any polypeptide comprising SEQ ID NO: 1 or any amino acid sequence having at least 90% sequence identity to SEQ ID NO: 1. Applicants respectfully traverse the rejection.

As previously discussed, Applicants assert specific utility for a polypeptide comprising the amino acid sequence of SEQ ID NO: 1 based on chemical and structural homology to NPT1, and the known function of NPT1, namely transport of phosphate molecules across cellular membranes. Homology to sequences of known function is a commonly used and reliable technique in the art for elucidating function. See Bonneau et al., 2001, *J. Struc. Biol.*, 134:186-190 at 187; Brenner et al., 1998, *Proc. Natl. Acad. Sci.*, 95:6073-6078. (copy enclosed) Forty percent sequence identity has been found to be a reliable threshold for determining homology for sequence alignments of at least 70 residues. Thirty percent sequence identity has been found to be a reliable threshold for determining homology for sequence alignments of at least 150 residues. See Brenner et al., supra, at 6076. SEQ ID NO:1 shares 48% sequence identity over

402 amino acids with NPT1. This level of homology exceeds Brenner et al.'s reliability threshold. Therefore, functional determination of SEQ ID NO:1 on the basis of sequence homology to NPT1, a known structure, is an accepted technique.

Moreover, as discussed previously, the specification provides detailed description and guidance for using the claimed antibodies. The specification describes use of the antibodies in diagnostic assays for conditions relating to an increase or decrease of NAPTR, in assays to detect increased or decreased expression of NAPTR in fluids and tissues from a subject, as an antagonist to NAPTR, and to target or deliver a pharmaceutical or agent to a cell expressing NAPTR.

Thus, Applicants submit that they have enabled how to use the claimed invention. Applicants respectfully request withdrawal of the rejection on this basis.

The Examiner rejected claims 11, 31, 32, 34, 42, and 43 under 35 U.S.C. § 112, first paragraph, as lacking an enabling disclosure. The Examiner stated that the specification is enabling for an antibody that specifically binds to the polypeptide SEQ ID NO:1. To expedite prosecution of the present application, claim 11 has been amended to recite an isolated antibody that specifically binds to a polypeptide comprising SEQ ID NO:1. However, Applicants expressly do not concede the propriety of the rejection and reserve the right to pursue claims corresponding to the subject matter within the scope of the subject matter of the claims as originally filed in a continuation application.

Withdrawal of the rejection is therefore respectfully requested.

2. Written Description

The Examiner rejected claims 11, 31, 32, 34, 42, and 43 under 35 U.S.C. § 112, first paragraph, as lacking adequate written description. The Examiner asserts that a genus of polypeptides comprising SEQ ID NO:1 and a genus of polypeptides comprising naturally occurring amino acid sequences at least 90% identical to SEQ ID NO:1 are not fully described in the specification. To expedite prosecution of the present application, claim 11 has been amended to recite an isolated antibody that specifically binds to a polypeptide comprising SEQ ID NO:1. However, Applicants expressly do not concede the propriety of the rejection and reserve the right

to pursue claims corresponding to the subject matter within the scope of the subject matter of the claims as originally filed in a continuation application.

Withdrawal of the rejection is therefore respectfully requested.

Rejection of Claims Under 35 U.S.C. § 102(e)

The Examiner rejected claims 11, 32, 34, 37, 38, 40, and 41 under 35 U.S.C. § 102(e) as anticipated by Feder et al. (U.S. Patent 5,872,237). As amended, independent claims 11, 37, and 40 recite an antibody that specifically binds a polypeptide comprising SEQ ID NO: 1. Claim 11 no longer recites a biologically active fragment of SEQ ID NO:1, an immunogenic fragment of SEQ ID NO:1, or a naturally occurring amino acid sequence that is 90% identical to SEQ ID NO:1. Claims 37 and 40 no longer recite an immunogenic fragment of SEQ ID NO:1.

Feder et al. does not teach a polypeptide comprising SEQ ID NO:1. For at least this reason, Feder et al. does not anticipate the claimed invention. Withdrawal of the rejection is respectfully requested.

Rejection of Claims Under 35 U.S.C. § 102(b)

The Examiner rejected claims 11, 32, 37, and 38 under 35 U.S.C. § 102(b) as anticipated by Dillner et al. (WO 91/18294). As amended, independent claims 11 and 37 recite an antibody that specifically binds to a polypeptide comprising SEQ ID NO:1. Claim 11 and 37 no longer recite an immunogenic fragment of SEQ ID NO:1. Dillner et al. does not teach a polypeptide comprising an amino acid sequence of SEQ ID NO: 1. Withdrawal of the rejection is respectfully requested.

Rejection of Claims Under 35 U.S.C. § 103(a)

The Examiner rejected claims 31, 42, and 43 under 35 U.S.C. § 103(a) as being obvious over Feder et al. in view of Krebber et al. (U.S. Patent 5,514,548). The Examiner asserts it would have been prima facie obvious to one of skill in the art to use the method of Krebber et al. to produce an antibody against the polypeptide of Feder et al. Applicants respectfully traverse the rejection.

Claims 31, 42, and 43 no longer recite a naturally occurring amino acid sequence that is 90% identical to SEQ ID NO:1. As amended, the claims recite an isolated antibody that specifically binds to a polypeptide comprising SEQ ID NO:1. Feder et al. does not teach or suggest an amino acid sequence of SEQ ID NO: 1 or antibodies that specifically bind to polypeptide comprising an amino acid sequence of SEQ ID NO: 1. Thus, this reference does not teach or suggest all of the limitations or elements of the claimed invention.

Krebber et al. does not cure the deficiencies of Feder et al. Krebber et al. discloses using recombinant techniques for generating antibodies and provides examples of chimeric and humanized antibodies. The reference, however, does not teach or suggest a polypeptide comprising SEQ ID NO:1. Because Krebber et al. does not teach or suggest a polypeptide comprising SEQ ID NO: 1, the references when combined do not disclose all of the elements or limitations of the claims.

Based on the forgoing, Applicants submit that Feder et al. in view of Krebber et al. does not teach or suggest the subject matter of the claims. Withdrawal of the rejection is therefore respectfully requested.

The Examiner rejected claims 31, 34, and 40-43 under 35 U.S.C. as obvious over Dillner et al in view of Krebber et al. The Examiner asserts it would have been prima facie obvious to one of skill in the art to use the method of Krebber et al. to produce an antibody against the immunogenic fragment of Dillner et al. Applicants respectfully traverse the rejection.

Claims 31, 34, and 40-43 no longer recite an immunogenic fragment of SEQ ID NO:1. As amended, the claims recite an isolated antibody that specifically binds to a polypeptide comprising an amino acid sequence SEQ ID NO: 1. Dillner et al. does not teach or suggest a polypeptide comprising SEQ ID NO:1 or antibodies that specifically bind a polypeptide of SEQ ID NO:1. Thus, the Dillner et al. reference does not teach or suggest all of the elements or limitations of the claimed invention.

Krebber et al. does not cure the deficiencies of Dillner et al. Krebber et al. discloses using recombinant techniques for generating antibodies and provides examples of chimeric and humanized antibodies. The reference, however, does not teach or suggest a polypeptide

comprising SEQ ID NO:1. Because Dillner et al. does not teach or suggest a polypeptide comprising SEQ ID NO: 1, these references in combination do not teach or suggest all of the elements of limitations of the claims.

Based on the forgoing, Applicants submit that Dillner et al. in view of Krebber et al. does not teach or suggest the subject matter of the claims. Withdrawal of the rejection is therefore respectfully requested.

Summary

Applicants submit the present application is in condition for allowance. Notice of such allowance is earnestly solicited. The Examiner is invited to contact the undersigned for clarification of any amendments and remarks or to otherwise facilitate prosecution of this application.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification

Please replace the title beginning at page 1, line 1, with the following title:

"Antibody Against Human [Novel] Sodium-Dependent Phosphate Cotransporter".

In the Claims

11. An isolated antibody that[which] specifically binds to [a polypeptide selected from the group consisting of:

a)] a polypeptide comprising the amino acid sequence of SEQ ID NO:1.[,

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1,

c) a biologically active fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1, and

d) an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1.]

37. A polyclonal antibody produced by a method [of claim 36] comprising:

(a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO:1;

(b) isolating an antibody from the animal; and

(c) screening the isolated antibody for specific binding to an amino acid sequence of SEQ ID NO:1.

40. A monoclonal antibody produced by a method [of claim 39] comprising:

(a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO:1;.

(b) isolating an antibody producing cell from the animal;

(c) fusing the isolated cell with an immortalized cell to form a hybridoma cell;

(d) culturing the hydridoma cell; and

(e) isolating from the hydridoma cell culture a monoclonal antibody that specifically binds an amino acid sequence of SEQ ID NO:1.